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Research Article

Smoked Food Consumption as Significant Risk Factor for Advanced Breast Cancer on Bone Scan in Southwest Nigerian Hospital

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ABSTRACT

The ingestion of smoked foods has been linked to the development of cancer. Polycyclic aromatic hydrocarbons have been recognized as carcinogenic compounds which contaminate smoked foods; their ingestion has been linked to the development of cancers such as breast cancer. Breast cancer may be evaluated using the nuclear bone scan as an imaging modality. This study reviewed bone scan results of patients with a positive history of consumption of smoked foods who presented at a Nuclear Medicine facility in South-West Nigeria. Our results show a significant association between a positive history of consumption of smoked foods and the presence of advanced breast cancer on the bone scan (($\chi 2 = 11.190$, $p = 0.001$, $df = 2$; Crude Odds Ratio (95% CI) = 1.692 (1.242-2.304). Thus, those patients with a history of eating smoked foods have between 50-100% increase in the risk of having abnormal scan findings. In a logistic regression, this association was retained (AOR=0.591 (0.434-0.805). Recommendations are made to address the significance of these findings.

Keywords: *Polycyclic Aromatic Hydrocarbons, Smoked foods, Diet, Breast Neoplasms, Nuclear Medicine, Radionuclide Imaging*

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INTRODUCTION

Breast cancer (BC) has been studied from many aspects in an attempt to better understand contributory aetiological factors and thus predict those at risk for developing it. Diet has been explored as a risk for developing BC. Findings from the literature suggest a direct link between the consumption of smoked food and the development of BC. (Parada *et al*., 2017) Smoked food and condiments are common staples of the local diet and contain polycyclic aromatic hydrocarbons (PAHs) which have been found to have a strong association with the development of BC. (Kotepui, 2016)

PAHs are ubiquitous organic chemicals of biogenic, petrogenic and pyrogenic origin. (US Environment Protection Agency;, 2013) This means that they may have their origins from biological, petroleum-related or combustive processes. Pyrogenic PAHs tend to have a higher percentage of parent PAH compounds as well as linearly configured ones. (Stout *et al*., 2015) They may be classified according to the number of rings that they possess, as their properties are related to this parameter. Boiling points increase proportionately from 200-600°C, while their vapour pressures and aqueous solubility are inversely related to the number of rings a PAH has. In addition, their toxicity increases in proportion to increasing molecular weight of these compounds. (Achten and Andersson, 2015)

The bone scan (BS) is an excellent staging modality that images the skeleton of BC patients before and after therapy, as well as in a monitoring capacity. Injected radioactive phosphonate compounds localize to the patient's bone matrix, thus enabling subsequent skeletal imaging thereafter. BS offers the advantage of a whole-body acquisition without necessitating administration of additional radiation. As the radioactive agent is incorporated into the phase of bone growth in bone matrix, the scan reflects osteoblastic bone lesions far more than osteolytic ones. BC metastases to bone are both osteoblastic and osteolytic in nature, and thus the BS has proved efficient in assessing BC. BS has a sensitivity of up to 95% for detecting bone lesions, and can detect changes in bone metabolism as low as 5%. (Hamaoka *et al*., 2004; Even-Sapir *et al*.; 2006) Its specificity is enhanced by taking into consideration patients' clinical history such as previous bone trauma, infection or inflammation and other pathology; as well as considering the pattern of lesions seen on the BS as normal, benign variants, benign disease or malignancy. Furthermore, three-dimensional nuclear tomography (single-

photon emission computed tomography (SPECT) or better yet hybrid single-photon emission computed tomography/computed tomography (SPECT/CT) aids localization of lesions on the scan. It also significantly reduces the frequency of equivocal lesions on the BS from 48-72% to as low as zero percent. (Even-Sapir *et al*., 2006; Helyar *et al*., 2010; Sharma *et al*., 2013)

This study presents the influence of smoked foods on the development of BC from a unique angle in the setting of Nuclear Medicine practice in a developing country. In this part of the world, we have found no previous study that has explored a possible association of ingestion of smoked foods and severity of BC involving nuclear bone scans. Thus, we sought to investigate any possible links between patients' consumption of smoked foods and the severity of BC as evidenced by BS findings

MATERIALS AND METHODS

This is a review of bone scans performed from January 2011 to December 2015 on BC patients; bone scans had been performed on these patients in order to determine the level of advancement of BC (staging). Data retrieved from their clinical records included dietary history indicating consumption of smoked food, smoking and/or alcohol intake. We also reviewed the results of their bone scans as (1) normal or with normal variants if they lacked evidence of skeletal metastases, (2) metastases if scan showed evidence of metastases and (3) equivocal if the lesions seen on BS could not be classified as benign or malignant without requiring complementary three-dimensional imaging or a follow-up bone scan.

We followed the universally accepted protocol of intravenous bolus injection of a radioactive bone-seeking compound (technetium-99m diphosphonate) followed by image acquisition with a single-head Siemens e.Cam gamma camera. A minimal delay of two hours was allowed between injection and imaging in order to afford uptake of radioactivity from the bloodstream to the skeleton. Findings were subjected to data analysis to determine the proportion of patients who reported ingestion of smoked food, and its influence on the level of disease progression of BC as evidenced by BS findings.

RESULTS

Selected patients in this study were all females as only eight patients were of the male gender among those who were referred for BS. These female patients with breast cancer were aged 24 - 85 years, with an average age of 49 ± 11.436 years. Patients were referred for BS from all geo-political regions of the country especially the South-West, with 26.9% of the patients resident in Lagos State

About two-thirds of patients' bone scans had abnormal findings (Table 1). Of those with abnormal findings, 263/497 (52.9%) had consumed smoked food while 234/497 (47.1%) did not have a history of eating smoked food. In a bivariate analysis there was an association between reporting a history of consumption of smoked food and having abnormal scan findings. This association is statistically significant ($\chi 2$ = 11.190, p = 0.001, df = 2; Crude Odds Ratio (95% CI) = 1.692(1.242-2.304). Thus, those patients with a history of eating smoked foods have between 50-100% increase in the risk of having abnormal scan findings. In a logistic regression, this association was retained (Adjusted Odds Ratio (95% CI) =0.591 (0.434-0.805).

In contrast, only three patients admitted to smoking while the others denied such a history. In addition, 57 patients (7.6%) had a history of imbibing alcohol; 26 regularly took some alcohol, 29 were social drinkers, two had stopped and 689 (92.4%) denied ever taking any. Thus, these parameters were not subjected to data analysis.

Representative whole-body bone scans of the participants are shown in Plates 1 and 2

DISCUSSION

Smoked foods are a staple of the local diet and are a regular ingredient in most local meals. Smoked, roasted, grilled and barbecued foods are also popularly consumed as readily available snacks and delicacies such as smoked plantain, corn, yam, meat (*suya, asun*) and fish. These foods are contaminated from the smoke generated during the process of preparation.

Table 1:
Association between bone scan findings and history of smoked food consumption

Diet group	Scan findings			COR (95% CI)	P	AOR (95% CI)
	Abnormal (%)	Normal (%)	Total			
History of smoked food	263 (72.7)	99 (27.3)	362 (100)	1.692 (1.242-2.304)	0.001	1
No history of smoked food	234 (61.1)	149 (38.9)	383 (100)			0.5 (0.436-0.805)
Total	497 (66.7)	248 (33.3)	745 (100)			

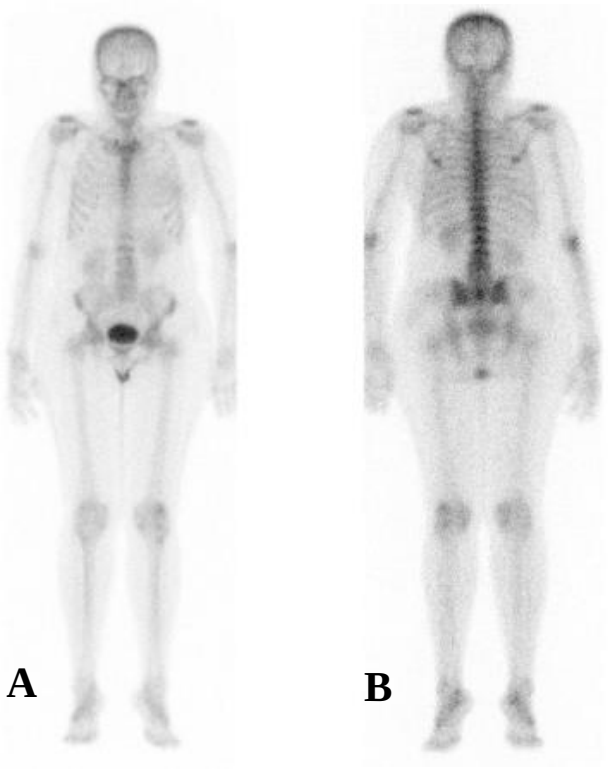

Plate 1:
Whole-body bone scan with no evidence of skeletal metastases. (A) Anterior image; (B) Posterior image

There are 16 prominent PAHs which have been recognized for their environmental toxicity by the Environmental Protection Agency (EPA), *viz* naphthalene, acenaphthylene, benzo[b]fluoranthene, phenanthrene, benzo[a]pyrene, dibenzo[a,h]anthracene, chrysene, acenaphthene, benzo[k]fluoranthene, fluorene, pyrene, benzo[a]anthracene, anthracene, fluoranthene, indeno[1,2,3-cd]pyrene, and benzo[g,h,i]perylene. (Stout *et al*., 2015; Tongo, Ogbeide and Ezemonye, 2017)

The influence of consumption of smoked food has been found a significant indicator of advanced BC in this cohort of patients. The relationship of smoked food with cancer has been traced to the presence of PAHs which are metabolized by heating and which then contaminate the food being prepared in this manner. Others have investigated the levels of PAHs in smoked foods and the carcinogenic link between consumption of smoked foods and breast cancer. (Akpambang *et al*., 2009; Parada *et al*., 2017; Tongo, Ogbeide and Ezemonye, 2017) Parada *et al* described their findings in which women with a greater consumption of grilled, smoked or barbecued food were relatively younger at diagnosis of BC than those who did not. In their cohort, the former group also had a higher alcohol intake rate.

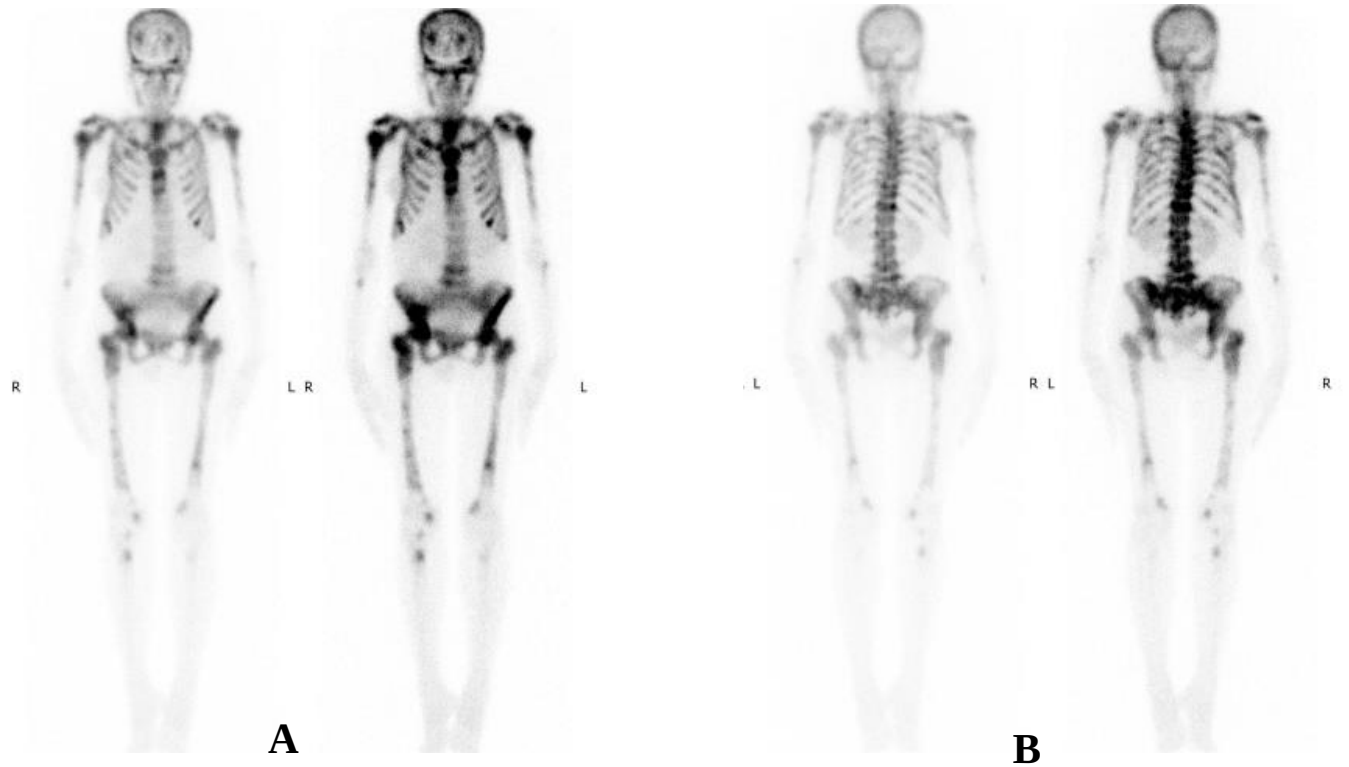

Plate 2:
Whole-body bone scan with widespread osteoblastic metastases involving axial and appendicular aspects of the skeleton. Images were duplicated and edited to emphasize presence of metastases. (A) Anterior image; (B) Posterior image.

A high pre-diagnosis rate of smoked and other similarly processed food consumption was associated with an increased mortality in these patients. Mortality also increased for those with continued consumption post-diagnosis. (Parada *et al*., 2017) The Working Group of the International Agency for Research on Cancer has classified processed foods including smoked meals as being carcinogenic to humans and creating a risk for colorectal cancer (Group 1), while unprocessed red meat was categorized as Group 2A being "probably carcinogenic to humans based on limited evidence". (Bouvard *et al*., 2015) .

We found no prior studies involving smoked food consumption and nuclear bone scans in the setting of BC in the literature at the time of writing up this research. As such, comparison with the results of previous studies using BS will not be possible. Our findings highlight the role that Nuclear Medicine plays in staging malignancies. Our results also reflect their largely late presentation in advanced stages of BC (approximately 67%), as has been consistently demonstrated in studies from this environment. (Awofeso *et al*., 2018; Dairo *et al*., 2018; Olarewaju, Oyekunle and Bamiro, 2019) This in turn has been linked with poorer outcome than in patients who presented timeously.

In conclusion, while there are regulatory agencies in developed countries, which have established maximal allowed levels of PAHs in foods, developing countries are not able to monitor the production of smoked foods in the same manner. For instance, the Codex Alimentarius comprises international food guides, standards and codes that govern "safety, quality and fairness" of international food trade. (FAO, 2019; Standard for smoked fish, smoke-flavoured fish and smoke-dried fish CXS 311- 2013, 2013) (Rodgers *et al*., 2000) Moreover, there is the Margin of Exposure (MOE), which "is a ratio of two factors which assesses for a given population the dose at which a small but measurable adverse effect is first observed and the level of exposure to the substance considered." (European Food Safety Authority, 2012; European Food Safety Authority Scientific Committee, 2012) Most of the food is smoked and sold by way-side vendors and is thus difficult to regulate. Thus, public enlightenment campaigns as well as periodic training and retraining of these vendors with safe preparation of smoked foods would be recommended. Smoked meat and fish are also viewed as culinary delicacies, which makes them even more popular. Publicity campaigns would also serve a double-pronged usefulness as they would educate the general populace (which includes cancer patients). For locally produced canned foods, the National Agency for Food and Drug Administration (NAFDAC) would also develop guidelines for maximal allowed proportions of PAH in food, as well as local equivalents of the Codex Alimentarius and the European Margin of Exposure. This will also guide the importation of canned smoked foods into the country. Nutritionists, dietitians as well as health workers should continue to promote the message of healthy living to patients, especially cancer patients.

With improving provision of electricity in this part of the world, there would be a dwindling dependence on smoking, grilling and roasting as a necessary means of food preservation. Being an epidemiological observational study, we did not discuss the mechanism by which ingestion of smoked foods by these patients led to the development of BC. The quantity of smoked food ingested was not stated in patients' clinical records, and thus could not be included in analysis of data

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